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Clinical benefits of joint mobilisation on ankle sprains: a systematic review and meta-analysis

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MAIN TEXT

Clinical Benefits of Joint Mobilisation on Ankle Sprains: A Systematic Review and Meta-Analysis

ABSTRACT

Objective: To assess the clinical benefits of joint mobilisation on ankle sprains.

Data sources: MEDLINE, MEDLINE In Process, Embase, AMED, PsycINFO, CINAHL, Cochrane library, PEDro, Scopus, SPORTDiscus and Dissertations and Thesis were searched from inception to June, 2017.

Study Selection: Studies investigating humans with a grade I or II lateral or medial sprains of the ankle in any pathological state from acute to chronic, who had been treated with joint mobilisation were considered for inclusion. Any conservative intervention was considered as a comparator. Commonly reported clinical outcomes were considered such as ankle range of movement, pain, and function. After screening of 1530 abstracts, 56 studies were selected for full text screening, and 23 were eligible for inclusion. Eleven studies on chronic sprains reported sufficient data for meta-analysis.

Data Extraction: Data were extracted using the participants, interventions, comparison, outcomes and study design approach. Clinically relevant outcomes (dorsiflexion range,

proprioception, balance, function, pain threshold, pain intensity) were assessed at immediate, short term and long term follow-up points.

Data Synthesis: Methodological quality was assessed independently by two reviewers and most studies were found to be of moderate quality, with no studies rated as poor.

Meta-analysis revealed significant immediate benefits of joint mobilisation compared to comparators on improving postero-medial dynamic balance (p=0.0004), but not for improving dorsiflexion range (p= 0.16), static balance (p = 0.96) or pain intensity (p= 0.45). Joint mobilisation was beneficial in the short term for improving weight-bearing dorsiflexion range (p= 0.003) compared to a control.

Conclusion: Joint mobilisation appears to be beneficial for improving dynamic balance immediately after application and dorsiflexion range in the short term. Long term benefits have not been adequately investigated.

Keywords: ankle sprains, chronic ankle instability, mobilisation, manual therapy, ankle joint

List of abbreviations:

ADL	activities of daily living
DFROM	dorsiflexion range of motion

FAAM	Foot and Ankle Ability Measure
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HVLA	high velocity low amplitude
M	males
MAT	Mulligan ankle taping
MCID	minimal clinically important difference
MD	mean difference
MWM	mobilisation with movement
PROSPERO	Prospective Register of Systematic Reviews
RICE	rest-ice-compression-elevation
RCT	randomised controlled trial
ROM	range of motion
SEBT	star excursion balance test
SMD	standard mean difference
TCJ	talo-crural joint
TFJ	tibio-fibular joint

Ankle sprains are a common injury in sports and the general community, and may lead to chronic pain, functional limitations and physical disability.[1, 2] Epidemiological studies

conducted in various countries highlight the high incidence of ankle sprains during sports training and competition with rates reported as 7 per 1000 in Denmark, 6.09 per 1000 in United Kingdom, and 2.15 per 1000 in the United States in person years.[3-5] Plantarflexion inversion sprain or lateral ankle sprain, is the most common type of ankle sprain.[6] It typically results in either an injury of the inferior tibiofibular ligament, anterior tibio-fibular ligament or the bifurcate ligament.[7] Eversion injuries often result in damage to the deltoid and spring ligaments of the medial aspect of the ankle.[7]

According to the Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability and Health from the Orthopaedic Section of The American Physical Therapy Association, manual therapy is recommended for both the acute and progressive loading phases of rehabilitation.[8] Management of ankle sprains commonly involves mobilisation procedures applied to the joint, such as non-thrust joint mobilisation, high velocity thrust manipulation, and mobilisation with movement (MWM).

The mechanisms by which these techniques are purported to work are biomechanical (such as stretching/tearing tissue, inducing cavitation within the joint, reducing muscle hypertonicity/stiffness) and neurophysiological, potentially including spinal cord and supra-spinally mediated mechanisms.[9, 10]

Several studies have investigated the effects of manual therapy on ankle sprains using a variety of outcome measures including pain, range of motion (ROM) and function from the acute to chronic stages of recovery, with different results reported.[11-21] Several systematic reviews have attempted to collate this evidence but have been limited by their narrow focus

on lateral ankle sprains and restricted outcome measures.[22-26] Previous systematic reviews have all included some studies which involved other interventions such as 'rest-ice-compression-elevation' (RICE) and home exercise programs, as an adjunct to mobilisation. Therefore, they have not actually assessed mobilisation as the sole intervention. Moreover, the clinical benefits of joint mobilisation have not yet been evaluated through meta-analysis, despite it being a common intervention used in the rehabilitation of a number of ankle conditions and despite the growing body of empirical literature.

The present systematic review aims to address these limitations by synthesising and meta-analysing the available evidence for ankle joint mobilisation (including high velocity thrust manipulation) in grade I or II ankle sprains of the medial or lateral ligaments in the acute/subacute/chronic stages of rehabilitation in any ambulant setting.

Methods

Registration

The protocol for this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on January 12, 2016 (CRD42016030194).

Search strategy

A search of electronic databases, including MEDLINE, MEDLINE In Process, Embase, AMED, PsycINFO, CINAHL, Cochrane library, PEDro, Scopus, SPORTDiscus, and

Dissertations and Thesis was conducted from inception to June, 2017. In addition to the database search, a hand search of the reference lists of identified studies was also carried out. A search strategy (Appendix 1) was developed for the main search strings of ankle sprain and mobilisation. Keywords used for 'ankle sprain' included sprain, talocrural joint, ligament injuries, lateral ligament, medial ligament, deltoid ligament, collateral ligament, anterior talo-fibular ligament, posterior talo- fibular ligament, sprain and strain, and ankle twist. Key words used for 'mobilisation' included manual therapy, joint mobilisation, manipulation, MWM, Maitland, Mulligan, and rehabilitation. These terms were used alone and in combinations during the search.

Identification and selection of studies

Full text randomised controlled trials, crossover studies, cross-sectional studies, cohort studies, and case series published in peer reviewed journals and dissertations were considered for the present review. Studies were not restricted by language, provided the title and abstract were in English. Studies not involving live human participants (e.g., model-based, animal and cadaveric investigations) were excluded. Conference proceedings, commentaries, research notes, editorials, and letters were also excluded. To be included, studies were required to meet the following criteria:

Participants

Live humans (without any age limitation) with a grade I or II lateral or medial ligament sprain of the ankle at any stage of recovery (acute to chronic) in any ambulant setting who have been treated with joint mobilisation. Studies involving grade III sprains, fractures (other than Weber type A), and syndesmotic injuries were excluded from this review.

Intervention

Studies reporting any type of joint mobilisation techniques applied to the talocrural joint, subtalar joint, or inferior tibiofibular joint by a physiotherapist, medical practitioner, osteopath, chiropractor or athletic trainer were eligible for inclusion in the review. Interventions other than therapist performed joint mobilisation were excluded from the review.

Comparators

Studies reporting any conservative intervention for comparison, such as exercise therapy, elevation and icing, supportive strapping, sham intervention, or no treatment, were eligible for inclusion. Control groups with healthy subjects were also eligible as a comparator. Studies which compared mobilisation techniques to surgical interventions were excluded.

Outcome measures

All commonly reported clinical impairments (pain, swelling, balance, proprioception, strength, stability, and gait), activity restriction and self-reported confidence, community participation, quality of life, re-injury rate, function, and return to sport were considered for the review. The primary outcomes of interest were ankle ROM, pain, quality of life, and function.

Timing of the measurement of the outcomes was categorised as either 'immediate', measured immediately following the intervention [27], 'short term' measured up to 3 months following the intervention [28], and 'long term' measured at 3 or more months [22] following the intervention.

Identified studies were exported to reference management software (EndNote X7.3.1, Ontario, Canada) and duplicate records were manually removed. Study titles and abstracts were initially screened by two independent reviewers, followed by screening of full text papers, to determine the eligibility of the identified studies. Disagreement between the reviewers was resolved by consensus or involvement of a third reviewer. The level of agreement between reviewers was assessed using Cohen's Kappa.[29]

Assessment of methodological quality

The methodological quality of individual studies was assessed using the PEDro scale for randomised controlled trials and the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies. [30-32] Two independent reviewers assessed the methodological quality and the level of agreement between reviewers was assessed using Cohen's Kappa.

Assessment of the quality of evidence

The overall quality of evidence was assessed at the stage of meta- analysis, using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. [33] The quality of the evidence was classified as either high, moderate, low, or very low. [34] Risk of

bias, consistency of results, directness (e.g. generalizability) and precision (e.g. sufficient data) were considered in assessing the overall quality. [35]

Data extraction and statistical analysis

Descriptive data were extracted using an extraction table (Table 1). Authors were contacted if possible where there were difficulties extracting data from the published paper. Where feasible, study data that were comparable in terms of participant characteristics, outcome measures and follow-up periods, were pooled and a meta-analysis was performed.

For the meta-analysis, the standard mean difference (SMD) was calculated for the outcomes where the means and standard deviations were provided pre- and post-intervention. This conversion of the data to a common scale permitted comparison of studies that used different tools to measure the same outcome. This review followed the general practice of interpretation for small, medium, and large effect sizes (0·2= small effect, 0.5= medium effect, 0.8= large effect).[36, 37] The mean difference (MD) was calculated for studies using the same instrument for measurement. The results were reported in forest plots with 95% CI. The minimal clinically important difference (MCID) was used to interpret the clinical meaningfulness of the findings. Inconsistency was quantified by calculating I^2 and interpreted as follows: 30% to 59% may represent moderate heterogeneity, 60% to 89% substantial heterogeneity, and 90% to 100% considerable heterogeneity between studies. If I^2 was greater than 30%, a random effects model was used to incorporate intertrial heterogeneity.[31]

In the instance of multiple comparison groups, the sham group was selected as the control condition. For the outcome of 'static balance', studies with eyes closed balance were selected

to maintain the homogeneity of the analysis. Further, in studies with multiple time points, measurements taken at 2-3 weeks were selected for the meta-analysis (e.g., if effects were measured at the time points of 2 days, 3 weeks and at 2 months in a single study, data from measurements at 3 weeks were selected for the analysis). All statistical analyses were conducted using RevMan 5.3, Copenhagen. [38]

Results

Selection and characteristics of included studies

The database search identified 1521 studies after duplicate removal and a further nine studies were identified through citation tracking and hand searching of reference lists (Figure 1). Following the first stage of screening (using study title and abstract), 56 studies (database search- n=47, hand search- n=9) were identified as eligible for inclusion from the original 1530 (database search- n=1521, hand search- n=9) studies. Common reasons for exclusion following title and abstract screening included; ineligible study design, joint mobilisation was not assessed in isolation, and the study aim was not relevant to the review research question. A further 33 studies were excluded in second stage (full text) screening, and reasons for exclusion included; study aim not relevant to research question [12, 18, 19, 39-54] (n=19), conference proceedings, commentaries and research notes[55-61] (n=7), not peer reviewed[62-64] (n=3), full text not available[65, 66] (n=2), study protocol only[67] (n=1), and thesis removed as the relevant published paper was included[68] (n=1). Twenty-three studies (including three theses) were therefore included in the current review. The inter-reviewer agreement for the title/abstract and full text screenings was considered to be very good (k=0.80, 95% CI 0.72-0.89) and good (k=0.71, 95% CI 0.52-0.90) respectively. All disagreements were resolved by

consensus. The data from 11 studies (including two theses[69, 70]) were available and deemed appropriate for inclusion in the meta-analysis (Figure 1). Publication bias was visually observed using funnel plots (Appendix 2).

The included studies were conducted in seven countries (Australia, Canada, Iran, New Zealand, South Africa, Spain, and United States) and involved a total of 585 participants. Twenty- one studies evaluated chronic ankle sprains and three studies investigated subacute sprains. Outcomes measured varied widely and included dorsiflexion range of motion (DFROM), proprioception, stability/balance, pain threshold (pressure and thermal), pain intensity and quality, function, talar stiffness, postural sway, and patient confidence. A range of joint mobilisation techniques were used and these included MWM in both weight-bearing or/and non weight-bearing (n=6)[13-16, 21, 71], antero-posterior talocrural mobilisation (Maitland grades III and IV)[72], (n=4)[69, 70, 73, 74], high velocity low amplitude (HVLA) ankle axial elongation manipulation and manipulation of the talocrural joint (n=6)[15, 75-79], Mulligan ankle taping (MAT) (n=3)[80-82], distal tibiofibular joint manipulation or mobilisation (n=2)[83, 84], and combined mobilisation and traction of the talocrural joint (n=4)[75, 85-87]. MAT was included because it aims to mimic a MWM by sustaining the fibula glide during daily activities. [7] These techniques were variously applied by physiotherapists, medical practitioners, chiropractors and athletic trainers. Table 1 describes the participants, interventions, comparators, outcome measures and results of the included studies.

The immediate effects of joint mobilisation were evaluated in 17 studies, short term effects in 10 studies, and the long term effects were assessed in only one study (Table 1). No studies evaluating effects on gait parameters, quality of life, re-injury rate or strength were located in

our search. In this systematic review, participants with chronic ankle sprains were included in 21 studies and three studies included participants with sub-acute sprains. No studies measuring the effectiveness of mobilisation in isolation for acute ankle sprains were able to be found. A meta-analysis was conducted using 11 studies, all involving participants with chronic ankle sprains.

Common mobilisation techniques used in rehabilitation of ankle sprains

Five combinations of mobilisation techniques were used in the 23 studies, including Mulligan MWM and taping techniques, Maitland mobilisation with and without traction, and manipulation. The number of studies with positive effects on any clinically relevant outcome are contrasted against the number of studies with no positive effects, for each mobilisation technique (Figure 2). The findings also suggest that the combination of Mulligan MWM and taping is more likely to produce a clinical benefit than the other three mobilisation combinations, as more (17) of the studies using MWM techniques found positive outcomes compared to other techniques (Maitland mobilisation 12, manipulation 14). Further, studies reporting no positive outcomes with MWM techniques are fewer in number (6) compared with the other techniques (Maitland mobilisation 14, manipulation 13).

Quality of studies

Due to differences in study design, two tools were used to assess the methodological quality of the included studies. PEDro was used for the assessment of randomised controlled trials (n =19) and the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies was used for all other study types (n =4). The level of agreement between reviewers for the

quality assessment was considered to be high (k = 0.63, 95% CI= 0.53-0.73) and all disagreements were resolved by consensus.

Most studies scored well on random allocation, adequate follow-up, and for providing both point measures and measures of variability for at least one key outcome. In studies assessed using the PEDro scale (Figure 3), the most common risk of bias was for therapist and subject blinding. For the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, all four studies demonstrated bias in terms of insufficient timeframe, different levels of exposures as related to the outcome examined, and clearly defined valid and reliable exposure measures (Figure 4). All studies scored at least moderate in terms of the overall quality of the methodology for both the scales utilised (Appendix 3-4).

Effects of mobilisation on sub-acute/chronic ankle sprains

The outcome measures of DFROM, proprioception, stability/balance, pain threshold, pain intensity and quality, function, talar stiffness, postural sway, and patient's confidence towards stability were assessed at varying time points across the studies after application of joint mobilisation. Table 2 lists each outcome evaluation, indicating positive effects of mobilisation at each of the three time points of interest.

Eleven studies on chronic sprains reported quantitative data on five different outcomes, including weight-bearing DFROM, static balance, dynamic balance, pain intensity and pain threshold. However, due to study heterogeneity and a lack of useable data for some outcomes, data could only be pooled for weight-bearing DFROM, static balance, dynamic balance and pain intensity in order to evaluate immediate effects, and weight-bearing

DFROM was the only outcome measure available to assess the short term effects of ankle mobilisation.

Immediate effects of mobilisation on ankle sprains

The immediate effects on DFROM were assessed in 14 outcome evaluations, of which 11 reported improvement with mobilisation techniques (Table 2). The findings for other outcomes were less notable. Of the 10 studies which investigated the immediate effects of mobilisation on stability/balance, three had demonstrable improvement.[14, 74, 81] Similarly, studies which assessed pain, talar stiffness and function revealed inconsistent results. When considering the immediate effects of mobilisation on functional outcomes, two outcome evaluations out of six demonstrated that it was effective.[80, 86] A summary of the reported immediate effects is provided in Table 2.

Pooled data from five studies with a total of 180 participants were grouped for analysis of the effects of mobilisation on each direction of the Star Excursion Balance Test (SEBT); anterior, postero-medial, and postero-lateral. This analysis provided significant findings for the postero- medial direction of the SEBT (MD= 3.22, CI= 1.43-5.01, p= 0.0004), however the postero- lateral direction (MD= 3.55, CI= -0.18- 7.28, p= 0.06) and the anterior direction (MD= 4.10, CI= -0.35- 8.54, p= 0.07) results of the SEBT, were not significant (Figure 5). Pooled data for static balance from three studies with a total of 100 participants indicated there were no significant immediate benefits following mobilisation of individuals with chronic sprains, when compared to control participants (SMD= 0.01, CI= -0.38-0.40, p= 0.96) (Figure 6).

Similarly, data from seven studies with a total of 249 participants indicated there were no significant immediate effects of mobilisation on the weight-bearing DFROM of individuals with chronic sprains (SMD= 0.66, CI= -0.25-1.58, p= 0.16) (Figure 7). For pain intensity, pooled data from two studies with a total 47 participants indicated mobilisation had no immediate effect on individuals with chronic sprains (SMD= -0.21, CI= -0.78-0.37, p= 0.48) (Figure 8). There were insufficient data to analyse the immediate benefits of mobilisation on pain threshold.

Short term effects of mobilisation on ankle sprains

Half of the outcome evaluations reported that mobilisation improved DFROM, stability/balance and pain threshold in the short term (Table 2). Demonstrable improvement was also observed in pain intensity and function (Table 2), and two studies[77, 85] which evaluated short term outcomes on talar stiffness and proprioception reported improvements. No studies reported short term findings on postural sway or patient's balance confidence.

Pooled data from two studies with 94 participants with chronic sprains indicated joint mobilisation was effective in the short term for improving weight-bearing DFROM (MD=2.56, CI=0.89- 4.23, p=0.003) (Figure 9). There were insufficient data evaluating static balance, dynamic balance, pain threshold and pain intensity to permit analysis of the short term benefits of mobilisation on these outcomes.

Long term effects of mobilisation on ankle sprains

Only one study evaluated the long term effects of mobilisation on ankle sprains. Long term improvement in DFROM and stability/balance were reported in the single included study.[14]

Quality of evidence

According to the GRADE assessment (Appendix 5), the evidence for DFROM (immediate and short term), static balance and dynamic balance can be considered to be of moderate quality. The evidence for pain was considered to be of low quality due to lack of generalisability of one of the included studies. Overall, the evidence included in this meta-analysis was considered to be of moderate quality, with the risk of bias and the level of heterogeneity the main factors influencing the quality of the evidence.

Discussion

This is the first systematic review to assess the clinical benefits of joint mobilisation in the management of either lateral or medial ankle ligament sprains at all stages of recovery. Importantly, this is the first review to only include studies in which joint mobilisation is the sole intervention. The current review did not identify any studies evaluating the clinical benefits of joint mobilisation on acute ankle sprains, perhaps because mobilisation is not typically the preferred choice of management in the acute stage of ankle sprains.[88] Findings about the clinical benefits of mobilisation on the majority of outcome measures were inconsistent across studies, and a lack of reported quantitative data, heterogeneity of subjects and the differing types of joint mobilisation applied made direct comparisons difficult. Despite this, meta-analysis indicated there are immediate benefits of mobilisation for

365 improving dynamic balance, and a short term benefit in improving weight-bearing DFROM
366 in chronic ankle sprains. These results provide compelling evidence that joint mobilisation
367 may be effective in improving balance immediately and in increasing dorsiflexion range of
368 motion in the short term in chronic ankle sprains.

369

370 Dynamic balance and weight-bearing DFROM improvements following joint mobilisation
371 were both associated with clinically meaningful changes. The modified SEBT test assesses
372 performance during single-leg balance with reaching in three directions (anterior, postero-
373 medial, postero- lateral).[89, 90] The MCID for this test is reported as being 3.5%, and therefore
374 the immediate effect on dynamic balance found in the meta-analysis (MD = 3.73) can be
375 considered as clinically meaningful.[89, 90] It is plausible that the immediate improvements in
376 dynamic balance following joint mobilisation may increase the individual's balance
377 confidence and perhaps reduce the risk of re-injury. Clinically, this may assist the individual
378 with an ankle sprain to more safely proceed to the next level of functional exercise in the
379 rehabilitation process.

380

381 There were no immediate improvements in either anterior SEBT performance or DFROM.
382 Interestingly, previous research supports the existence of a correlation between anterior
383 SEBT performance and the weight-bearing lunge test[91]. This correlation could help explain
384 the current review's findings on immediate anterior SEBT performance and DFROM.
385 Notably, the MCID for ankle DFROM has not been established.[92] However, approximately
386 3.6° of DFROM is associated with 1 cm in distance from the wall in the lunge test.[74] The MD
387 in the short term measurement of weight-bearing DFROM from the current meta-analysis

388 was 2.56 cm and this equates to 9.2° of dorsiflexion, which can be considered as clinically
389 meaningful given that the normal total range is only 15- 20°. [93, 94]

390

391 Joint mobilisation techniques are aimed at restoring the normal joint ROM[95, 96], and indeed
392 this review found DFROM improved following mobilisation. However, the mechanisms by
393 which restoring ankle ROM may assist other impairments is unclear, as are the underlying
394 mechanisms by which mobilisation may actually work.[15, 16] It has been proposed that
395 increased ankle ROM is due to the correction of a bony positional fault.[10] It is further
396 postulated that the correct alignment of the articular surfaces may help to restore normal
397 biomechanics, as well as sensorimotor function[10]. However, it may be that mobilisation
398 produces less impact on pain, as evidenced by the lack of improvement in ankle pain outcome
399 measures in this review. Potential underlying central nervous system changes related to
400 persistent pain in chronic sprains remain unclear, but central sensitization may be a possible
401 factor for persistence of chronic pain. If central sensitization is actually a key factor
402 contributing to chronic ankle sprain pain, then changing the bony alignment would be
403 unlikely to improve pain in chronic sprains as it is not the usual localized pressure pain
404 hypersensitivity[97] experienced immediately after a sprain.

405

406 According to the Clinical Practice Guidelines Linked to the International Classification of
407 Functioning, Disability and Health from the American Physical Therapy Association,
408 clinicians should use joint mobilisation to improve ankle dorsiflexion, proprioception, and
409 weight-bearing tolerance in patients recovering from a lateral sprain.[8] Of these three
410 outcomes, the findings of the current review only support the benefit of mobilisation for
411 dorsiflexion. There was insufficient research available to conclude whether mobilisation is

effective for improving proprioception or weight-bearing tolerance. However, the current review found clinically meaningful evidence for the effect of mobilisation on dynamic balance, an outcome not mentioned in the Clinical Practice Guidelines from the American Physical Therapy Association. One explanation for this difference may be that the Guidelines only included literature published prior to April 2012, while the current review has included seven more recently published studies.

The inclusion and exclusion criteria of the current review differ in important ways from previous systematic reviews on this topic. In contrast to these prior reviews, our search criteria included both lateral and medial ligament sprains, covered all stages of recovery from acute to chronic, and encompassed all clinically relevant outcomes used to assess the effects of mobilisation. Importantly, of the six prior reviews which have evaluated the efficacy of mobilisation techniques on ankle sprains, all included studies which did not evaluate joint mobilisation as a unique intervention, but rather as an adjunct to other interventions (such as home exercise programs, RICE protocol and external supports included in their review.[22, 24-27, 98] The current review excluded these multi-modal studies to ensure the homogeneity of the included studies, and to increase the precision of the results in relation to the effects of joint mobilisation. Compared to the recent review by Loudon et al,[24] the present review included almost three times more studies (23), with all of these only investigating the clinical effects of joint mobilisation techniques in isolation. In the review by Loudon et al,[24] only eight studies were included, and of those mobilisation was used as the sole intervention in only five.[24] This disparity in the number of included studies may be due to our searching a greater number of databases (11), including medial ankle sprains in the search criteria, by reviewing dissertations and theses, and by not limiting clinical outcomes.

436

437 This review includes the first meta-analysis undertaken to assess the clinical benefits of joint
438 mobilisation for ankle sprains. When comparing the findings of the current review to
439 previous systematic reviews, there were some agreements and some inconsistent results.
440 When considering the immediate effects of mobilisation, the review by van der Wees et al[26]
441 reported an improvement in DFROM.[26] However, the current review did not support an
442 immediate effect on weight-bearing DFROM, with mobilisation providing only a short term
443 effect. Pain and function are concluded to improve immediately in the review by Southerst et
444 al [27], but in our review immediate pain relief was not evident and inconclusive results were
445 found for immediate function. When considering the short term effects, the effectiveness of
446 mobilisation in increasing ankle ROM was supported in the review of Bleakely et al[22], and
447 this was consistent with the findings of the current review. [22] The review by van Ochten et
448 al[28] reported positive changes in short term pain and function in chronic sprains, however the
449 findings of the present review were inconclusive for both of these outcomes.[28] When
450 considering the long term effects of mobilisation, pain and function are improved according
451 to the review by Southerst et al.[27] The findings of the current review on these outcomes were
452 inconclusive due to lack of data. Different definitions of inclusion criteria for mobilisation
453 techniques included within reviews (e.g., including other therapies such as home exercise or
454 RICE treatment along with mobilisation), as well as differences in the databases searched and
455 the periods of the data searches, are all factors contributing to these differing findings.

456

457 Study Limitations

458 Limitations of this review include the wide variation in follow-up time points that we defined
459 as short term (from one day to less than three months). Additionally, the included studies

have used a range of different mobilisation techniques and comparators. It was beyond the scope of this review to attempt to determine the independent merits of individual techniques. In particular, there may be value in analysing joint mobilisation and high velocity thrust manipulation techniques separately rather than together, but given the lack of available research at this time directly comparing these two manual therapy approaches this level of scrutiny is not possible. In addition, it was not possible to pool data to analyse the effectiveness of mobilisation for some important outcomes that were reported in single studies. Despite attempts to contact authors of included studies, data were insufficient to analyse immediate effects on pressure pain threshold and short term effects on pressure pain threshold and pain intensity. Finally, no high quality evidence was found, to provide robust evidence for the effectiveness of joint mobilisation for ankle sprains.

Further research is required to determine the mechanisms by which mobilisation improves dynamic balance and weight-bearing DFROM. Also, the long term effects of mobilisation on ankle sprains should be further investigated using clinically relevant outcomes.

Conclusions

Joint mobilisation appears to clinically benefit individuals with chronic ankle sprains, improving dynamic balance immediately and weight-bearing DFROM in the short term. It is unlikely to have an immediate effect on static balance, pain intensity, and weight-bearing DFROM. Other clinical outcomes that have been reported following mobilisation demonstrate an inconsistent response to mobilisation, and this may be a reflection of previous study designs or of the intervention itself.

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Figure legends

Figure 1: Flow chart of study selection

Figure 2: Percentage and number of outcome evaluations with and without positive findings following each technique combination of mobilisation for any clinically relevant outcome at any time point

Figure 3: PEDro scores for assessment of quality of individual criteria[30]

1, eligibility criteria were specified (*Explanation: This criterion influences external validity, but not the internal or statistical validity of the trial. It has been included in the PEDro scale so that all items of the Delphi scale are represented on the PEDro scale. This item is not*

used to calculate the PEDro score) (PEDro Scale); 2, participants were randomly allocated to groups; 3, allocation was concealed; 4, groups were similar at baseline regarding most important prognostic indicators; 5,blinding of all participants; 6, blinding of therapists who administered the therapy; 7, blinding of all assessors who measured at least one key outcome; 8, measures of at least one key outcome were obtained from more than 85% of the participants; 9, all participants for whom outcome measures were available received the treatment or control condition as allocated; 10, results of between group statistical comparisons are reported for at least one key outcome; 11, study provides both point measures and measures of variability for at least one key outcome

Figure 4: Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[32]

1, Research question or objective clearly stated; 2, Study population clearly specified and defined; 3, Participation rate of eligible persons ≥50% ; 4, Subjects selected from same or similar population; 5, Sample size justification; 6, Exposure(s) of interest measured prior to outcome(s); 7,Timeframe sufficient; 8, Different levels of exposures as related to the outcome are examined; 9, Exposure measures clearly defined, valid, and reliable;10, Exposure(s) assessed more than once over time; 11,Outcome measures clearly defined, valid, and reliable; 12, Outcome assessors blinded to the exposure status; 13, Follow up after baseline ≤20% ; 14, Adjusted for potential confounding variables

Total (0 to 14)

Figure 5: MD (95% CI) of the immediate effect of joint mobilisation on dynamic balance by pooling data from five studies (n = 180). CI, confidence interval; SD, standard deviation; MD, mean difference; SEBT, star excursion balance test

Figure 6: SMD (95% CI) of the immediate effect of joint mobilisation on static balance by pooling data from three studies (n = 100). CI, confidence interval; SD, standard deviation; SMD, standard mean difference

Figure 7: SMD (95% CI) of the immediate effect of joint mobilisation on weight-bearing DFROM by pooling data from seven studies (n = 249). CI, confidence interval; SD, standard deviation; SMD, standard mean difference; weight-bearing DFROM, weight-bearing dorsiflexion range of movement

Figure 8: SMD (95% CI) the immediate effect of joint mobilisation on pain intensity by pooling data from two studies (n = 47). CI, confidence interval; SD, standard deviation; SMD, standard mean difference

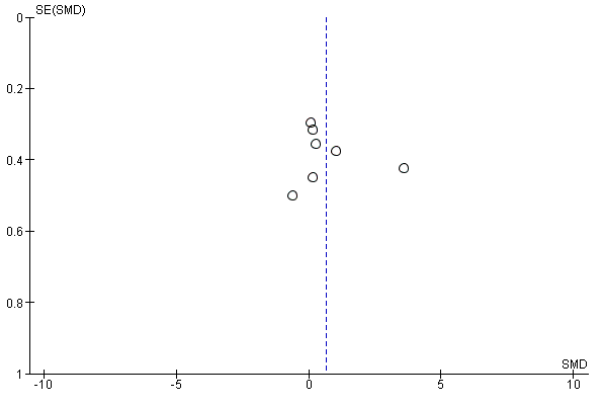
Figure 9: MD (95% CI) of the short term effect of joint mobilisation on weight-bearing DFROM by pooling data from two studies (n = 94). CI, confidence interval; SD, standard deviation; MD, mean difference; weight-bearing DFROM, weight-bearing dorsiflexion range of movement

#	Searches
1	Ankle Injuries/
2	ankle sprain.mp.
3	(ankle* adj5 injur*).tw.
4	(ankle* adj5 sprain*).tw.
5	(ankle* adj5 twist*).tw.
6	(injur* adj5 ligament*).tw.
7	lateral ligament*.mp. or Collateral Ligaments/
8	Ankle Joint/ or medial ligament*.mp.
9	Ankle Joint/ or deltoid ligament*.mp.
10	ATFL.mp.
11	PTFL.mp.
12	"Sprains and Strains"/
13	talo crural.tw.
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15	Chiropractic/ or Manipulation, Orthopedic/
16	musculoskeletal manipulation.mp. or Musculoskeletal Manipulations/
17	(joint* adj5 manipul*).tw.
18	(ankle* adj5 rehab*).tw.
19	Mulligan*.mp.
20	Maitland*.mp.
21	MWM*.mp.
22	manual therap*.mp.
23	manual technique*.mp.
24	(joint* adj5 mobili?ation*).tw.
25	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

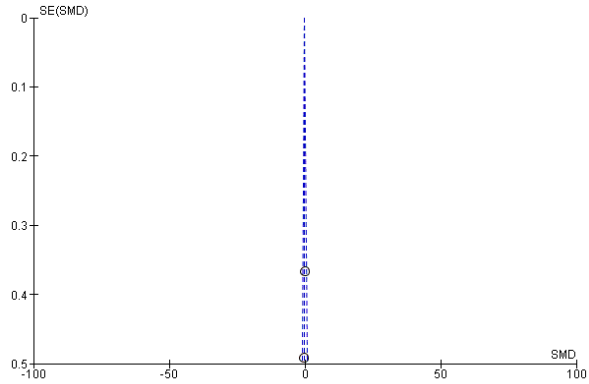
26	Randomized controlled trial.pt.
27	clinical trial.pt.
28	random*.tw.
29	trial*.tw.
30	group*.tw.
31	case series.tw.
32	cross-over studies/
33	Cross-Sectional Studies/
34	exp Cohort Studies/
35	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
36	14 and 25 and 35
37	limit 36 to humans

Funnel plots

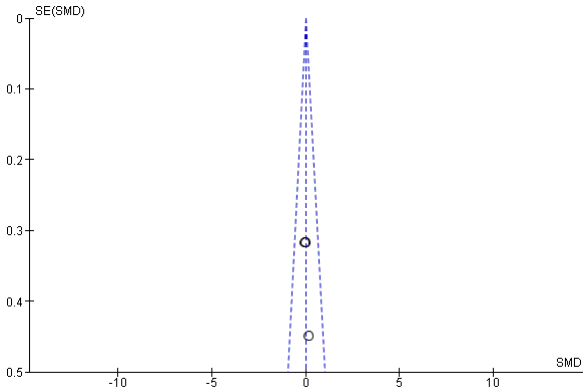
Immediate effect of mobilisation on weight-bearing dorsiflexion, pain, static balance and dynamic balance



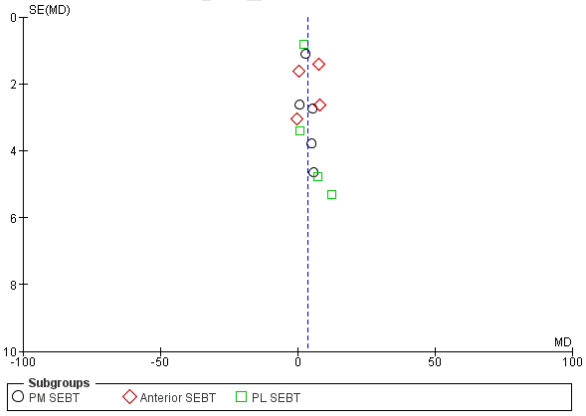
a) Weight-bearing dorsiflexion



b) Pain

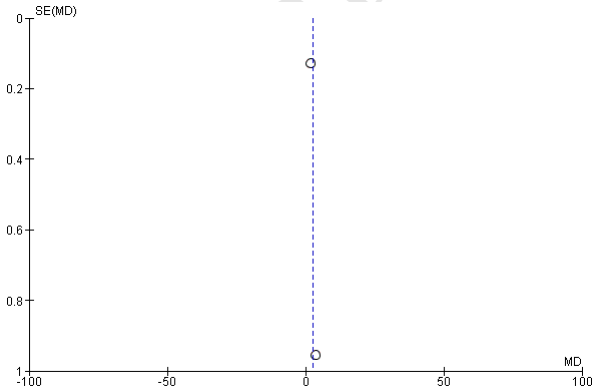


c) Static balance



d) Dynamic balance

Short term effect of mobilisation on weight-bearing dorsiflexion



a) Weight-bearing dorsiflexion

SE=Standard Error; SMD=standard mean difference; MD=mean difference, PM =postero-medial; PL postero-lateral; SEBT star excursion balance test

PEDro scores for assessment of quality of individual intervention studies

	PEDro scale											
Study	1) Eligibility criteria	2) Random allocation	3) Concealed allocation	4) Baseline comparability	5) Blinding subjects	6) Blinding therapists	7) Blinding assessors	8) Adequate follow-up (than 85% of subjects)	9) Intention to treat analysis	10) Between-group comparisons	11) Point measures and variability	Total Score out of 10
Alanson 2012	+	+	+	-	-	-	+	+	+	+	+	7
Beazell, Grindstaff et al. 2012	+	+	-	+	-	-	+	+	+	+	+	7
Collins, Teys et al. 2004	+	+	-	+	+	-	+	+	-	+	+	7
Cruz-Diaz, Lomas Vega et al. 2015	+	+	+	+	-	-	+	+	-	+	+	7
Harkey, McLeod et al. 2014	+	+	+	+	-	-	+	+	+	+	+	8
Hoch and McKeon 2011	+	+	+	+	-	-	+	+	+	+	+	8
Hopper, Samsson et al. 2009	+	+	-	+	-	-	-	+	+	+	+	6
Joseph, de Busser et al. 2010	+	+	+	+	-	-	-	+	+	+	+	7
Kohne, Jones et al. 2007	+	+	+	-	-	-	-	+	+	+	+	6

Lopez-Rodriguez, de-Las-Penas et al. 2007	+	-	-	+	-	-	-	+	+	+	+	5
Marron-Gomez, Rodriguez-Fernandez et al. 2015	+	+	-	+	+	-	+	+	+	+	+	8
Pellow and Brantingham 2001	+	+	-	+	-	-	-	+	-	+	+	5
Plante 2012	+	+	-	+	-	-	-	+	+	+	+	6
Reid, Birmingham et al. 2007	+	+	-	+	-	-	+	+	-	+	+	6
Someeh, Norasteh et al. 2015	+	+	-	+	-	-	-	+	+	+	+	6
Someeh, Norasteh et al. 2015	+	+	-	+	-	-	-	+	+	+	+	6
Vicenzino, Branjerdporn et al. 2006	+	+	-	+	+	-	+	+	+	+	+	8
Wells 2012	+	+	+	+	-	-	+	+	+	+	+	8
Yeo and Wright 2011	+	+	-	+	-	-	+	+	+	+	+	7

+ meet criteria, - do not meet criteria

1, eligibility criteria were specified (*Explanation: This criterion influences external validity, but not the internal or statistical validity of the trial. It has been included in the PEDro scale so that all items of the Delphi scale are represented on the PEDro scale. This item is not used to calculate the PEDro score*) (PEDro Scale); 2, participants were randomly allocated to groups; 3, allocation was concealed; 4, groups were similar at baseline regarding most important prognostic indicators; 5,blinding of all participants; 6, blinding of therapists who administered the therapy; 7, blinding of all assessors who measured at least one key outcome; 8, measures of at least one key outcome were obtained from more than 85% of the participants; 9, all participants for whom outcome measures were available received the treatment or control condition as allocated; 10, results of between-group statistical comparisons are reported for at least one key outcome; 11, study provides both point measures and measures of variability for at least one key outcome 1

Reference

1. PEDro-scale. 1999. Retrieved 05.12.2015. Available from: URL: http://www.pedro.org.au/english/downloads/pedro-scale/.

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies scores for assessment of quality of individual cohort studies

Study	Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies scale														Score out of 14
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
(Gilbreath, Gaven et al. 2014)	+	+	+	+	+	-	-	-	+	+	+	-	+	+	10
(Hoch, Andreatta et al. 2012)	+	+	+	+	+	-	-	-	+	+	+	+	+	+	11
(Hoch, Mullineaux et al. 2014)	+	+	+	+	+	-	-	-	+	+	+	-	+	+	10
(Houston, McKeon et al. 2013)	+	+	+	+	-	-	-	-	+	-	+	-	+	-	7

+ meet criteria, - do not meet criteria

1, Research question or objective clearly stated; 2, Study population clearly specified and defined; 3, Participation rate of eligible persons ≥50% ; 4, Subjects selected from same or similar population; 5, Sample size justification; 6, Exposure(s) of interest measured prior to outcome(s); 7,Timeframe sufficient; 8, Different levels of exposures as related to the outcome are examined; 9, Exposure measures clearly defined, valid, and reliable;10, Exposure(s) assessed more than once over time; 11,Outcome measures clearly defined, valid, and reliable; 12, Outcome assessors blinded to the exposure status; 13, Follow-up after baseline ≤20% ; 14, Adjusted for potential confounding variables Total (0 to 14)1, 2

References

1. National-Institutes-of-Health. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. 2014.

2. The-Cochrane-Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. 2011.

Assessment of the quality of evidence					
Number of studies (sample size, n)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence
Immediate effects					
Outcome: DFROM					
7 studies (n; experimental=126: control=123)	Low risk of bias (Pedro scores: 6,6,7,8,8,8 and 8)	p value on test for heterogeneity p<0.00001, I^2=91% High inconsistency	Low indirectness	Low imprecision	Moderate quality (low risk of bias and high inconsistency)
Outcome: dynamic balance					
5 studies (n; experimental=90: control=90)	Low risk of bias (Pedro scores: 6,7,8,8 and 8)	p value on test for heterogeneity p=0.02, I^2=52% Moderate inconsistency	Low indirectness	Low imprecision	Moderate quality (low risk of bias and moderate inconsistency)
Outcome: static balance					
3 studies (n; experimental=50: control=50)	Moderate risk of bias (Pedro scores: 6,6 and 8)	p value on test for heterogeneity p=0.93, I^2=0% Low inconsistency	Low indirectness	Low imprecision	Moderate quality (moderate risk of bias and low inconsistency)
Outcome: pain intensity					
2 studies (n; experimental=24: control=23)	Moderate risk of bias (Pedro scores: 5 and 8)	p value on test for heterogeneity p=0.73, I^2=0% Low inconsistency	Moderate indirectness (less generalisable)	Low imprecision	Low quality (moderate risk of bias, moderate inconsistency and low indirectness)
Short term effects					
Outcome: DFROM					
2 studies (n; experimental=48: control=46)	Low risk of bias (Pedro scores: 7 and 8)	p value on test for heterogeneity p<0.0001, I^2=95% High inconsistency	Low indirectness	Low imprecision	Moderate quality (low risk of bias and high inconsistency)

DFROM, Dorsiflexion range of movement

Table 1: Description of the eligible studies

Study	Design	Sample	Intervention and dosage	Comparator	Measurement time points	Outcomes	Results
Alanson et al, 2012[75]	RCT	17(10M) Grade 1/2 Chronic lateral ankle sprains	TCJ (antero-posterior)-mobilisation + TCJ traction 30s	Sham	Immediate	Non weight-bearing DFROM, proprioception (joint position sense)	Non weight- bearing DFROM, significantly improved across time- p=0.04, joint position sense significantly improved across time at target angle 10° PF -p=0.03
Beazell et al, 2012[84]	RCT	43 Chronic ankle sprains	Distal TFJ manipulation + HVLA thrust	No intervention	Immediate, short term (1 week, 2 weeks and 3 weeks*)	Weight bearing DFROM, static balance (single limb	Weight bearing DFROM not significant- p=0.82, single limb stance not significant- p=0.42, function not significant; ,step down test t - p=0.76,

			1 repetition			stance), function (step down test, self-reported function, FAAM sports)	self-reported function -p=0.61, FAAM sports -p=0.83
Collins et al, 2004[13]	Randomised cross over	16 (8M) Grade 2 Subacute lateral ankle sprains	Weight-bearing MWM TCJ (posterior talar glide, postero anterior tibial glide)	Placebo, No intervention	Immediate	Weight-bearing DFROM, pressure pain threshold, thermal pain threshold	Weight- bearing DFROM significantly improved-across time p=0.013 and no significant group difference (vs placebo -p=0.202, vs control-p=0.208), pressure pain threshold and thermal pain threshold - not significant-

			3 sets of 10 repetitions				p<0.05)
Cruz-Díaz et al, 2015[14]	RCT	81(47M) Chronic ankle sprains	Weight – bearing MWM TCJ (posterior talar glide, postero-anterior tibial glide-) 2 sets of 10 repetitions , 2 sessions per week	Sham, no intervention	Immediate, short term (3 weeks), long term (6 months)	Weight – bearing DFROM, dynamic balance (SEBT)	Weight –bearing DFROM significantly improved- p<0.0001(at each time point), dynamic balance significantly improved - p<0.0001(each direction of SEBT)

			for 3 weeks				
Gilbreath et al, 2014[21]	Prospective longitudinal	11(5M) Chronic ankle sprains	Weight – bearing MWM TCJ (posterior talar glide, postero anterior tibial glide) 2 sets of 4 repetitions 4m of	No control group	Short term (after 24-48 h)	Weight – bearing DFROM,dynamic balance (SEBT), function (FAAM)	Weight –bearing DFROM not significant- p=0.69, dynamic balance not significant- (SEBT- anterior p=0.99; postero-medial -p=0.15; postero-lateral p=0.24), FAAM ADL not significant, p=0.19, FAAM SPORTS significantly improved across time- p=0.01

			MWM X 3 sessions over a 1 week				
Harkey et al, 2014[73]	RCT	30 (14M) Chronic ankle sprains	Maitland mobilisation TCJ (antero-posterior grade III) 3 sets of 60s	No intervention	Immediate	Non weight-bearing DFROM, dynamic balance (SEBT)	Non weight- bearing DFROM significantly improved (p= 0.049), dynamic balance no improvement- p >0.05
Hoch & McKeon, 2011[74]	Randomised cross over	20(9M) Chronic ankle sprains	Maitland mobilisation TCJ- (anterior	No intervention	Immediate	Weight-bearing DFROM, static balance	Weight- bearing DFROM significantly improved –p=0.01, static balance significantly improved, Time to boundary antero-posterior

			posterior III) $50^{+}/_{-}5$ of 1s oscillations X2			dynamic balance (SEBT), talar stiffness	minima significant improved- =p<0.0001 , dynamic balance-not significant- p=0.98 (normalised reach distance) talar stiffness not significant-p=0.08
Hoch et al, 2012[87]	Prospective longitudinal	12(6M) Chronic ankle sprains	Maitland mobilisation TCJ (antero-posterior III)+ TCJ traction 2 sets of 2m traction and 4 sets of 2m mobilizatio	No control group	Short term (24–48 h and one week follow-up)	Weight bearing DFROM,dynamic balance, function (FAAM)	Weight bearing DFROM significantly improved across time- p<0.0001, dynamic balance significantly improved across time- (SEBT anterior- p<0.0001); postero-medial- p=0.003; postero-lateral- p<0.0001), FAAM ADL and SPORTS significantly improved across time- p=0.001

			n				
Hoch et al, 2014[85]	Prospective longitudinal	12 (6M) Chronic ankle sprains	Maitland Mobilisation TCJ (antero posterior III) + TCJ traction 2 sets of 2mtraction and 4 sets of 2m	No control group	Short term (24–48h, and one week follow-up)	Static balance, talar stiffness	Static balance not significant; time to boundary antero-posterior and time to boundary medio-lateral not significant- p >0.05 , talar stiffness not significant-p>0.05
Hopper et al., 2009[82]	Randomised controlled Within-	20 (8M) Chronic ankle sprains	Mulligan ankle taping Not explicitly	Injured taped, Injured un-taped,	Immediate	Static balance ,dynamic balance (wandering,	Static balance significantly improved in postural sway recovery across time - p<0.001; single limb stance not significant- 0.792,

	subjects design		stated	Uninjured taped, Uninjured un-taped		overshoot, reaction time)	dynamic tracking balance not significant ; wandering- p=0.559, overshoot- p=0.547, reaction time- p=0.142
Houstan et al, 2013[86]	Prospective longitudinal	12 (6M) Chronic ankle sprains	Maitland mobilisation TCJ (antero-posterior III) + TCJ traction 4m of traction and 8m of mobilisation 6 sessions	No control group	Immediate ,short term (one week follow-up)	Function (FAAM sports)	FAAM ADL some components significantly improved across time; walking on even ground- p= 0.06; going down stairs-p = 0.07; walking on uneven ground- p= 0.03; light to moderate work- p =0.06; heavy work- p = 0.03; recreational activity- p= 0.07, FAAM SPORTS some components significantly improved across time; landing- p = 0.03; low impact activities- p = 0.07; cutting- p

			over 2 weeks.				= 0.02
Joshep et al., 2010[99]	RCT	40(19M) Grade 1/2 Chronic lateral ankle sprains	Ankle axial elongation TCJ (superior inferior)- HVLA thrust 6 sessions over 3 weeks	Muscle energy technique	Short term (one month)	DFROM,plan tarflexion range of motion, static balance, pain quality and intensity, function (functional evaluation scale)	DFROM significantly improved across time (p<0.001) and no significant group differences(p=0.713), plantarflexion range of motion significantly improved across time (p<0.001) and no significant group differences (p=0.300), single limb stance eyes closed significantly improved across time (p<0.001) and no significant group differences (p=0.344), single limb stance eyes open significantly improved across time

							(p<0.001) and no significant group differences (p=0.413), McGill significantly improved across time (p<0.001) and no significant group differences (p=0.077) Functional evaluation scale significantly improved across time (p<0.001) and no significant group differences (p=0.144)
Kohne, et al 2007[77]	RCT	30(21M) Grade 1/2 Chronic recurrent lateral ankle sprains	Ankle axial elongation TCJ(superior inferior by a mortise separation)-	Single manipulation treatment	Short term (fifth week follow-up)	DFROM, proprioception (joint position sense), pressure pain	DFROM significantly improved- p=0.028 (across time) , Joint position sense at 5° plantarflexion error significantly improved-

			6 manipulations over 4 weeks)			threshold, pain intensity	p= 0.029 (across time) pressure pain threshold (p value not reported), pain intensity (p value not reported)
Lopez-Rodrıguez et al, 2007[79]	Randomised controlled within-subject repeated measures	52 (35M) Grade 2 Chronic lateral ankle sprains	TCJ Manipulation (Caudal) HVLA thrust + posterior gliding manipulation TCJ - HVLA thrust 1m	Placebo	Immediate	Proprioception	Proprioception significantly improved ; load support bilateral posterior load-p=0.016, anterior load-p=0.04, posterior load-p=0.043, posterior anterior load-p=0.016

Marron-Gomez, 2015[15]	RCT	52 (31M) Chronic ankle sprains	Weight – bearing MWM TCJ (posterior talar glide, postero-anterior tibial glide) 1 set of 10 repetitions TCJ HVLA distraction thrust x3	Placebo	Immediate, short term (24 and 48 hrs)	Weight bearing DFROM	MWM-Weight bearing DFRFOM significantly greater than placebo- $p < 0.05$ (immediately and short term) HVLA- Weight bearing DFROM significantly greater than placebo- $p<0.001$(immediately) and $p=0.001$(short term)

Pellow et al., 2001[78]	RCT	30(19M) Grade 1/2 sub-Acute and chronic lateral ankle sprains	Ankle axial alongation (TCJ-superior inferior by a mortise separation) 8 manipulations over 4 weeks	Detuned ultrasound treatment	Short term (one month follow up)	Non weight-bearing DFROM, pain threshold, pain quality and intensity, function (functional evaluation scale)	Non weight- bearing DFROM significantly improved across time-p=0.001 and between groups-p=0.001, ,pain threshold significantly improved across time-p=0.002 and no significant group differences -p=0.395, McGill significantly improved across time-p=0.001 and between groups-p=0.004, , pain intensity significantly improved across time-p=0.002 and between groups-p=0.004, functional evaluation scale significantly improved across time-

							p=0.001 and between groups- p<0.001
Plante, 2012[70]	RCT	20(12M) Chronic ankle sprains	TCJ (antero-posterior) 10 oscillations	Healthy subjects	Immediate	Weight bearing DFROM, static balance, function (dynamic functional tasks)	Weight bearing DFROM significantly improved across time p<0.0001, single limb stance; centre of pressure significantly improved -p<0.04, dynamic functional task (centre of pressure medial- lateral during jump task significantly improved p<0.001; centre of pressure medial-lateral during squat significantly improved p< 0.022; centre of pressure medial –lateral during stance task significantly improved-

							p<0.0.039)
Reid et al, 2007[71]	Randomised cross over	23(8M) Chronic lateral ankle	Weight-bearing MWM (posterior talar glide, postero-anterior tibial glide) 10 repetitions X2	Sham	Immediate	Weight bearing DFROM	Weight bearing DFROM significantly improved-p=0.02

Someeh et al, 2015[81]	Experimental study design- within subjects	32(20M) Chronic ankle sprains	Mulligan ankle taping/Fibular repositioning taping Not explicitly stated	Healthy subjects	Immediate	Dynamic balance (SEBT)	Dynamic balance significantly improved across time- SEBT overall reach - p=0.001
Someeh et al, 2015[80]	Experimental study design- within subjects	32(20M) Chronic ankle sprains	Mulligan ankle taping Not explicitly stated	Healthy subjects	Immediate	Function (dynamic functional tasks), participants perceptions of stability	Function significantly improved across time; single leg hopping- p=0.014; figure of 8 hopping- p=0.05; side hopping- p=0.001), confidence in above mentioned functional tests significantly

						and confidence	improved across time consequently p=0.023, 0.048, and 0.038
Vicenzino et al, 2006[16]	Randomised cross over	16(8M) Chronic lateral ankle sprains	Non weight bearing-MWM (antero posterior talar glide for DF), 4 glides of 10s 4 sets Weight bearing MWM (posterior	No intervention	Immediate	Weight bearing DFROM, talar stiffness	Weight bearing DFROM significantly improved-p=0.017, talar glide significantly improved-p<0.001

			talar glide, postero anterior tibial glide) 4 sets of 10 glides				
Wells, 2012[69]	RCT	17 (7M) Chronic ankle sprains	Maitland mobilisation (TCJ- antero-posterior IV) 3 repetitions, 60s	No intervention	Immediate	Weight -bearing DFROM, Non weight -bearing BDFROM, dynamic balance, pain intensity, static	Weight -bearing DFROM not significant- p=0.95, Non weight -bearing DFROM not significant- p=0.1, dynamic balance not significant; SEBT composite- p=0.8; anterior - p=0.07; postero-medial- p=0.79; postero lateral- p=0.73, pain not significant- p=0.06, stiffness not significant- p=0.59,

						balance, stiffness, function (self-reported function)	stability not significant- p=0.40), function (VAS) not significant- p=0.44
Yeo et al, 2011[83]	Randomised controlled within-subject repeated measures	13(10M) Grade 2 Subacute lateral sprain	Maitland mobilisation (distal TFJ antero-posterior) 3 sets of 1m mobilisation	Placebo, No intervention	Immediate	Weight bearing DFROM, pressure pain threshold, pain intensity, function (functional evaluation scale)	Weight bearing DFROM significantly improved- p<0.0001, pressure pain threshold significantly improved- p<0.0001, pain intensity not significant- p=0.369, functional evaluation scale not significant- p=0.475

ADL= activities of daily living; DFROM= dorsiflexion range of motion; FAAM= Foot and Ankle Ability Measure; HVLA= high velocity low amplitude; M-Male; MWM- mobilisation with movement; RCT = randomised controlled trial; SEBT = Start Excursion Balance Test; TCJ= talocrural joint; TFJ = tibio-fibular joint

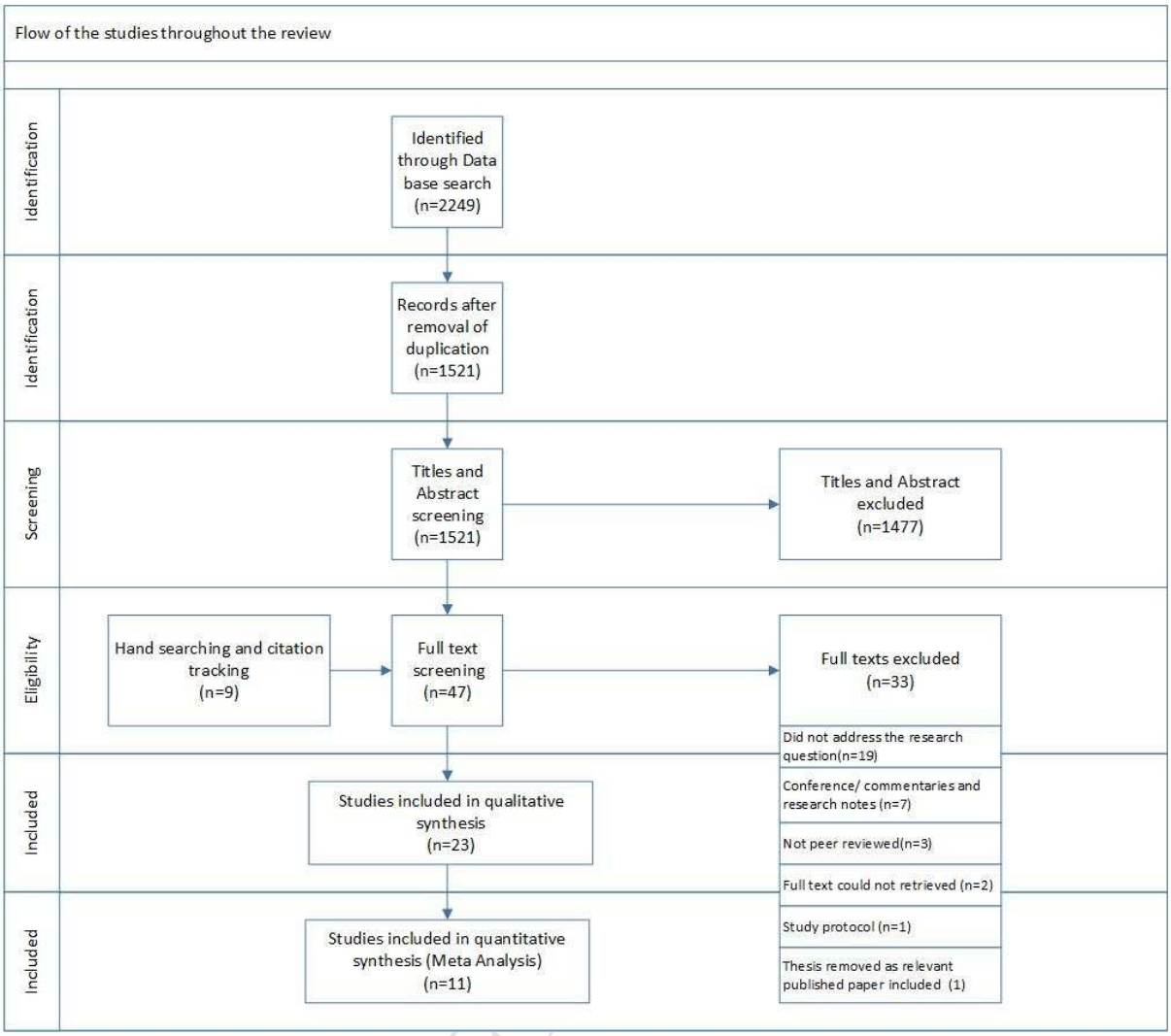
'Immediate': measured immediately following the intervention, 'Short term': measured up to 3 months following the intervention, 'Long term': measured at 3 or more months following the intervention

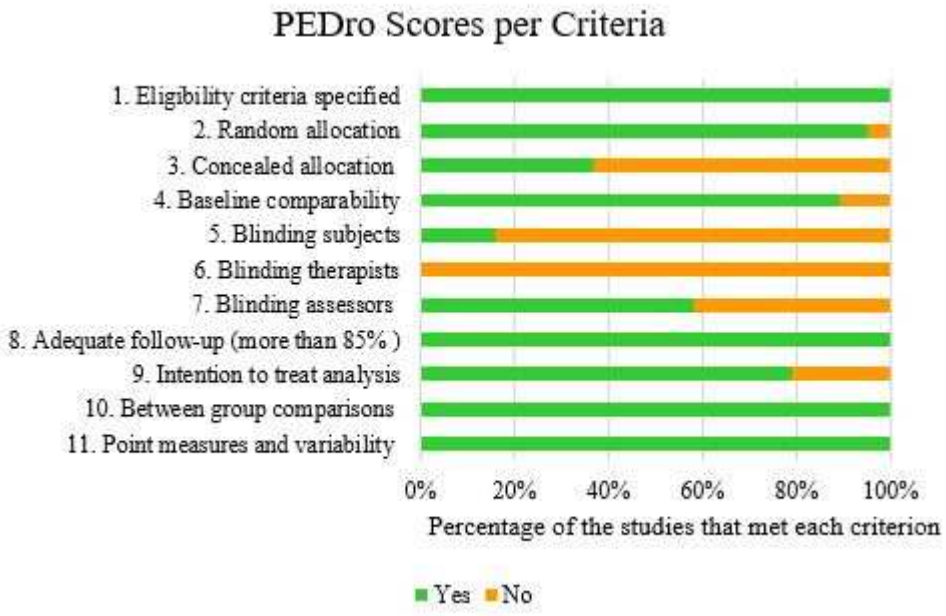
Table 2: Number of outcome evaluations investigating at each time point of interest, listed by the reported positive effects

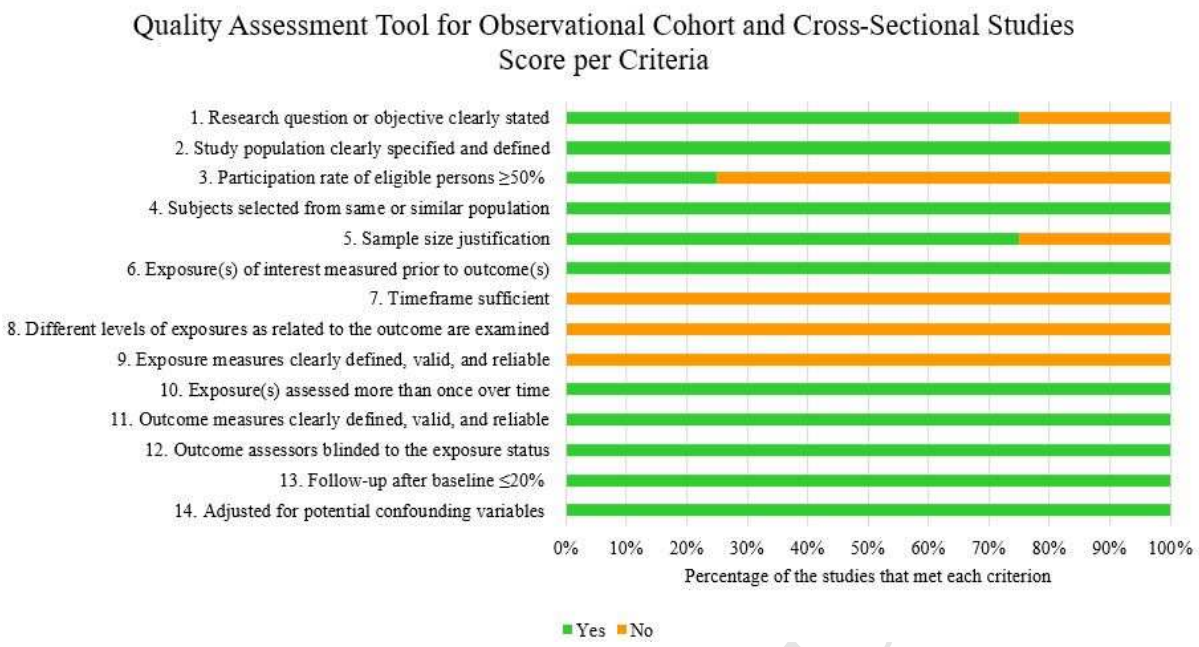
Outcome	Positive findings					
	Immediate		Short term		Long term	
	Yes	No	Yes	No	Yes	No
1. DFROM	11	3	4	4	1	0
Weight bearing DFROM	9	2	3	2	1	0
Non weight bearing DFROM	2	1	0	1	0	0
Unspecified	0	0	1	1	0	0
2. Proprioception	2	0	1	0	0	0
3. Stability/balance	3	7	3	3	1	0
Static balance	1	3	1	3	0	0
Dynamic balance	2	4	2	0	1	0
4. Pain threshold	1	1	1	1	0	0
5. Pain intensity	0	2	2	1	0	0
6. Functional outcomes	2	4	4	2	0	0
7. Talar stiffness	1	2	0	1	0	0
8. Recovery from postural sway	1	0	0	0	0	0
9. Patient's confidence towards stability	1	0	0	0	0	0

DFROM=dorsiflexion range of motion

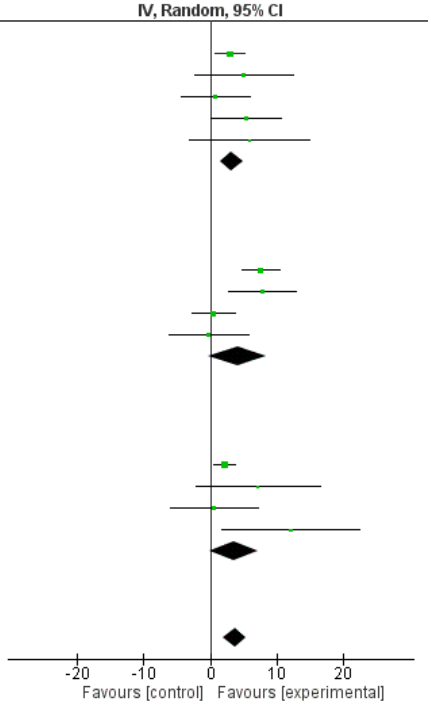
'Immediate': measured immediately following the intervention, 'Short term': measured up to 3 months following the intervention, 'Long term': measured at 3 or more months following the intervention





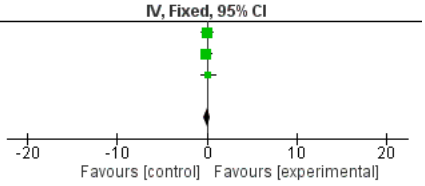


Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 Postero-medial SEBT								
Cruz-diaz et al, 2015(14)	88.51	5.43	30	85.52	2.86	31	14.7%	2.99 [0.80, 5.18]
Harkey et al, 2014(73)	83	11	15	78	9.7	15	4.2%	5.00 [-2.42, 12.42]
Hoch & McKeon, 2011(74)	94.06	8.15	20	93.3	8.48	20	7.1%	0.76 [-4.39, 5.91]
Someeh et al, 2015(81)	101.8	8.3	16	96.4	7.2	16	6.7%	5.40 [0.02, 10.78]
Wells, 2012(69)	85.04	7.55	9	79.12	11	8	3.1%	5.92 [-3.16, 15.00]
Subtotal (95% CI)			**90**			**90**	**35.8%**	**3.22 [1.43, 5.01]**
Heterogeneity: Tau² = 0.00; Chi² = 2.11, df = 4 (P = 0.72); I² = 0%								
Test for overall effect: Z = 3.52 (P = 0.0004)								
1.2.2 Anterior SEBT								
Cruz-diaz et al, 2015(14)	84.72	5.07	30	77.09	6.01	31	12.8%	7.63 [4.84, 10.42]
Harkey et al, 2014(73)	72.5	7.5	15	64.6	6.8	15	7.1%	7.90 [2.78, 13.02]
Hoch & McKeon, 2011(74)	79.44	4.73	20	78.91	5.51	20	11.6%	0.53 [-2.65, 3.71]
Wells, 2012(69)	64.82	6.12	9	65.07	6.42	8	5.8%	-0.25 [-6.23, 5.73]
Subtotal (95% CI)			**74**			**74**	**37.4%**	**4.10 [-0.35, 8.54]**
Heterogeneity: Tau² = 15.83; Chi² = 14.94, df = 3 (P = 0.002); I² = 80%								
Test for overall effect: Z = 1.80 (P = 0.07)								
1.2.3 Postero-lateral SEBT								
Cruz-diaz et al, 2015(14)	89.28	3.04	30	87.11	3.25	31	16.5%	2.17 [0.59, 3.75]
Harkey et al, 2014(73)	77.6	13.9	15	70.4	12.2	15	2.9%	7.20 [-2.16, 16.56]
Hoch & McKeon, 2011(74)	87.48	10.55	20	86.89	11.02	20	5.0%	0.59 [-6.10, 7.28]
Wells, 2012(69)	82.65	10.04	9	70.47	11.57	8	2.4%	12.18 [1.82, 22.54]
Subtotal (95% CI)			**74**			**74**	**26.8%**	**3.55 [-0.18, 7.28]**
Heterogeneity: Tau² = 5.81; Chi² = 4.80, df = 3 (P = 0.19); I² = 37%								
Test for overall effect: Z = 1.87 (P = 0.06)								
Total (95% CI)			**238**			**238**	**100.0%**	**3.73 [2.00, 5.46]**
Heterogeneity: Tau² = 4.06; Chi² = 24.83, df = 12 (P = 0.02); I² = 52%								
Test for overall effect: Z = 4.23 (P < 0.0001)								
Test for subgroup differences: Chi² = 0.14, df = 2 (P = 0.93), I² = 0%								



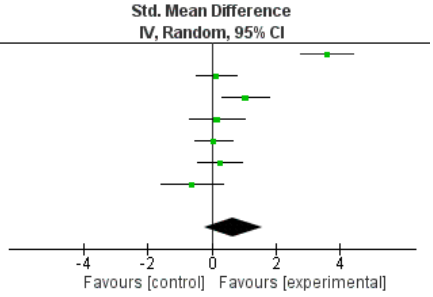
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Hoch & McKeon, 2011(74)	1.96	0.6	20	1.95	0.45	20	40.0%	0.02 [-0.60, 0.64]
Hopper et al, 2009(82)	3.23	1.06	20	3.31	1.26	20	40.0%	-0.07 [-0.69, 0.55]
Plante, 2012(70)	1.028	0.029	10	1.024	0.024	10	20.0%	0.14 [-0.73, 1.02]
Total (95% CI)			**50**			**50**	**100.0%**	**0.01 [-0.38, 0.40]**

Heterogeneity: Chi² = 0.15, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)



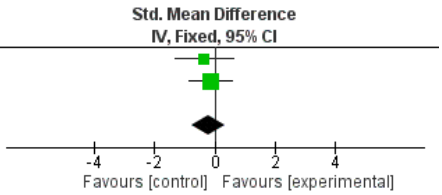
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cruz-diaz et al, 2015(14)	16.8	0.47	30	15.07	0.48	31	14.0%	3.59 [2.77, 4.42]
Hoch & McKeon, 2011(74)	12.62	2.79	20	12.2	3.01	20	14.8%	0.14 [-0.48, 0.76]
Marron-Gomez, 2015(15)	11.5	3.8	18	8.3	1.5	15	14.4%	1.04 [0.31, 1.78]
Plante, 2012(70)	13	3	10	12.4	4	10	13.9%	0.16 [-0.72, 1.04]
Reid et al, 2007(71)	10.55	3.79	23	10.32	3.89	23	14.9%	0.06 [-0.52, 0.64]
Vicenzino et al, 2006(16)	4.8	1.5	16	4.4	1.6	16	14.5%	0.25 [-0.44, 0.95]
Wells, 2012(69)	9.5	2.73	9	11.04	1.93	8	13.4%	-0.61 [-1.59, 0.37]
Total (95% CI)			**126**			**123**	**100.0%**	**0.66 [-0.25, 1.58]**

Heterogeneity: $Tau^2 = 1.37$; $Chi^2 = 64.78$, df = 6 ($P < 0.00001$); $I^2 = 91\%$
Test for overall effect: $Z = 1.42$ ($P = 0.16$)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Pellow et al, 2001(78)	1.96	2.06	9	2.76	2.4	8	35.7%	-0.34 [-1.30, 0.62]
Wells, 2012(69)	2.87	1.65	15	3.07	1.28	15	64.3%	-0.13 [-0.85, 0.58]
Total (95% CI)			**24**			**23**	**100.0%**	**-0.21 [-0.78, 0.37]**

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.48)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cruz-diaz et al, 2015(14)	17.04	0.48	30	15.12	0.52	31	49.7%	3.79 [2.93, 4.64]
Marron-Gomez, 2015(15)	12	3.7	18	8.3	1.5	15	50.3%	1.24 [0.48, 1.99]
Total (95% CI)			**48**			**46**	**100.0%**	**2.50 [0.00, 5.00]**

Heterogeneity: Tau² = 3.08; Chi² = 19.13, df = 1 (P < 0.0001); I² = 95%
Test for overall effect: Z = 1.96 (P = 0.05)